IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

N RE APPLICATION OF:	
Liu & Villarete	EXAMINER: M. Mosher
APPLICATION NO.: 10/824,710	ART UNIT: 1648
FILED: April 14, 2004	CONFIRMATION NO.: 7146
FOR: **METHOD OF TREATMENT USING INTERFERON-TAU**	

DECLARATION OF DR. NORMAN KACHUCK UNDER 37 C.F.R. § 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Norman J. Kachuck, declare:

1. I am presently an Associate Professor of Clinical Neurology at the University of Southern California Keck School of Medicine. I have been on the faculty of USC since 1991. I am a co-director of the Neuroimmunology Division of the Department of Neurology.

2. I am currently the Director of the Multiple Sclerosis (MS) Comprehensive Care Center at the University of Southern California. I oversee the MS group's clinical research activity as well as spearheading the disease management aspects of the Center mission.

3. I serve on the board of the Clinical Advisory Committee of the National MS Society.

4. I obtained a medical degree in 1987 from the University of Southern California School of Medicine. I also completed a residency in neurology at the Los Angeles County+University of Southern California Medical Center.

5. I have been active in the field of multiple sclerosis (MS) research for over 15 years, as a clinician and investigator in MS immunology and therapeutics. In addition to my clinical research, I have an active clinical practice, in addition to teaching medical students, allied health profession students, and doctors in training.

6. As a result of my experience summarized in points (1)-(5), I am knowledgeable about multiple sclerosis, including its diagnosis, progression, clinical presentation, and treatment.

7. I am a principal investigator in a nine-month clinical study to evaluate the safety and efficacy of orally administered interferon-tau on the symptoms and disease state of persons previously diagnosed with multiple sclerosis. As of this date, data is available for the first six months of the study.

8. In this study, twenty-three patients in an active disease state were selected for participation, of whom sixteen are currently evaluable. The disease status was classified as active based on the presence of a gadolinium-enhancing lesion observed in at least one of three magnetic resonance imaging (MRI) brain scans taken during a three month period prior to enrollment and treatment. Lesions, also known as plaques, are patches of inflammation in the central nervous system (CNS) in which tracts of nerve cells have been stripped of their myelin, an insulating fatty protein, as well as being damaged themselves. The axon extensions of the neurons, which comprise much of the so-called white matter of the brain and spinal cord, are responsible for sending communication signals both within the CNS and between the CNS and the rest of the body. Demyelinated neurons and damaged nerve fiber tracts do not function efficiently and it is this condition that gives rise to the symptoms of multiple sclerosis. Lesions can be observed with the aid of gadolinium, which targets new (inflammatory) lesions in the CNS. MRI scans of the brain after administration of gadolinium are used to assist in the diagnosis of multiple sclerosis, to monitor the status and progression of the disease after diagnosis, and to assess the response to patients to treatments.

9. The sixteen patients selected for the study received, via oral administration, 3.0 mg of interferon-tau three times per day, for a total daily dose of 9.0 mg. Based on a specific antiviral activity of 1-2 x 10^8 Units/mg protein, measured in a standard assay, the daily dosage given to each patient was between approximately 9 x 10^8 and 1.2 x 10^9 Units.

10. The reduction in new gadolinium-enhancing lesions was used as a clinical endpoint to evaluate the effectiveness of interferon-tau in treating the enrolled multiple sclerosis patients. MRI brain scans of each patient were taken monthly for six months to evaluate the number of new gadolinium-enhancing lesions. The MRI scans were read by expert MRI readers who manually established the location of the lesions. The number of new gadolinium-enhancing lesions was established by comparing the location of lesions on subsequent scans to the pretreatment scans.

11. The attached table summarizes the number of new gadolinium-enhancing lesions for fifteen of the initially-enrolled sixteen patients that remained in the study at the six month time point.

12. The average number of new gadolinium-enhancing lesions during the screening period (months -3, -2, and -1, prior to treatment) for the fifteen patients was 2.17. After six months of treatment, the average number of new gadolinium-enhancing lesions decreased to 1.30, a 62% decrease from the baseline, screening number of lesions.

13. When the results are analyzed in terms of individual patients, the treatment method was effective to substantially reduce the appearance of new contrast-enhanced lesions in 10 out of 15 patients, who had an excellent response to the treatment with a reduction in new lesions of 50% or more over the average number of new lesions during the screening, pretreatment period. Four patients (001, 007, 009 and 013) had a good response to the treatment with a reduction in the number of new

lesions was achieved. The remaining patient (015) had an increase in the number of new lesions.

14. The reduction in the number of new gadolinium-enhancing lesions observed in the patients treated with interferon-tau is an indicator of efficacy. It is expected that a reduction in brain lesions will be associated with a reduction in the clinical relapses, brain atrophy, and progressive disability which is expected to occur in multiple sclerosis patients.

15. My overall conclusion is that the ability of high-dose oral administration of interferon-tau to eliminate the appearance of new lesions in a majority of the patients with an active form of MS represents a significant and important improvement in treatment methods available for active MS. Moreover, the method has the potential to overcome many of the patient compliance issues and undesirable side effects associated with currently available treatment methods.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the Unites States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

Date: 12/18/05

Norman J. Kachuck, M.D.

Patient No.	Screen 1	Screen 2	Average Screen	No. of Gd-Enhancing Lesions Post-Treatment with Interferon-tau (month post treatment)						Average Gd-enhancing Lesions after treatment	Percent of reduction from screen average
				1	**2**	**3**	**4**	**5**	**6**		
001	6	19	12.5	10	4	6	5	0	30	9.16	26%
002	3	6	4.5	4	0	0	1	2	1	1.33	70%
003	0	1	0.5	0	0	0	0	0	0	0.00	100%
004	1	1	1	1	0	0	0	1	0	0.33	67%
005	2	0	1	0	0	0	0	0	0	0.00	100%
006	5	0	2.5	0	0	0	1	0	na**	0.20	92%
007	1	0	0.5	2	0	0	na	0	0	0.40	20%
008	1	0	0.5	0	0	0	0	1	0	0.16	67%
009	1	1	1	0	1	1	1	0	1	0.66	34%
010	0	3	1.5	0	1	1	0	0	0	0.33	78%
011	2	0	1	1	1	0	1	0	0	0.50	50%
012	3	1	2	0	0	0	2	2	na	0.80	60%
013	2	2	2	5	0	0	1	1	1	1.33	34%
014	3	1	2	1	na	1	2	0	0	0.80	60%
015	0	0	0	0	0	na	0	0	2	0.40	N/A

**na=MRI scan not done and data not available
N/A=not applicable